SEQUENCE LISTING



WEISGRABER, KARL H. FARESE, ROBERT V. RAFFAI, ROBERT DONG, LIMING

<120> GENE-TARGETED ANIMAL MODEL OF
 APOLIPOPROTEIN E4 DOMAIN INTERACTION AND USES THEREOF

<130> UCAL-222 <140> 10/017,718 <141> 2001-12-14 <150> 60/276,861 <151> 2001-03-16 <160> 13 <170> FastSEQ for Windows Version 4.0 <210> 1 <211> 299 <212> PRT <213> homo sapiens <400> 1 Lys Val Glu Gln Ala Val Glu Thr Glu Pro Glu Pro Glu Leu Arg Gln • 10 Gln Thr Glu Trp Gln Ser Gly Gln Arg Trp Glu Leu Ala Leu Gly Arg 20 25 Phe Trp Asp Tyr Leu Arg Trp Val Gln Thr Leu Ser Glu Gln Val Gln 40 Glu Glu Leu Leu Ser Ser Gln Val Thr Gln Glu Leu Arg Ala Leu Met 55 Asp Glu Thr Met Lys Glu Leu Lys Ala Tyr Lys Ser Glu Leu Glu Glu 75 70 Gln Leu Thr Pro Val Ala Glu Glu Thr Arg Ala Arg Leu Ser Lys Glu 90 85 Leu Gln Ala Ala Gln Ala Arg Leu Gly Ala Asp Met Glu Asp Val Cys 105 Gly Arg Leu Val Gln Tyr Arg Gly Glu Val Gln Ala Met Leu Gly Gln 125 120 Ser Thr Glu Glu Leu Arg Val Arg Leu Ala Ser His Leu Arg Lys Leu 135 140 Arg Lys Arg Leu Leu Arg Asp Ala Asp Asp Leu Gln Lys Arg Leu Ala 150 155 Val Tyr Gln Ala Gly Ala Arg Glu Gly Ala Glu Arg Gly Leu Ser Ala 165 170 Ile Arg Glu Arg Leu Gly Pro Leu Val Glu Gln Gly Arg Val Arg Ala 185 Ala Thr Val Gly Ser Leu Ala Gly Gln Pro Leu Gln Glu Arg Ala Gln 200 Ala Trp Gly Glu Arg Leu Arg Ala Arg Met Glu Glu Met Gly Ser Arg 215 Thr Arg Asp Arg Leu Asp Glu Val Lys Glu Gln Val Ala Glu Val Arg

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235
                 230
225
Ala Lys Leu Glu Glu Gln Ala Gln Gln Ile Arg Leu Gln Ala Glu Ala
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Phe Gln Ala Arg Leu Lys Ser Trp Phe Glu Pro Leu Val Glu Asp Met
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Gln Arg Gln Trp Ala Gly Leu Val Glu Lys Val Gln Ala Ala Val Gly
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Thr Ser Ala Ala Pro Val Pro Ser Asp Asn His
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Gln Ala Glu Trp Gln Ser Gly Gln Pro Trp Glu Leu Ala Leu Gly Arg
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Phe Trp Asp Tyr Leu Arg Trp Val Gln Thr Leu Ser Glu Gln Val Gln
                          40
Glu Glu Leu Leu Ser Pro Gln Val Thr Gln Glu Leu Thr Thr Leu Met
                       55
Asp Glu Thr Met Lys Glu Leu Lys Ala Tyr Lys Ser Glu Leu Glu Glu
                                    75
Gln Leu Ser Pro Val Ala Glu Glu Thr Arg Ala Arg Leu Ser Lys Glu
                                 90
Leu Gln Ala Ala Gln Ala Arg Leu Gly Ala Asp Met Glu Asp Val Arg
                             105
Ser Arg Leu Val Gln Tyr Arg Ser Glu Val Gln Ala Met Leu Gly Gln
                          120
Ser Thr Glu Glu Leu Arg Ala Arg Leu Ala Ser His Leu Arg Lys Leu
                      135
                                         140
Arg Lys Arg Leu Leu Arg Asp Ala Asp Asp Leu Gln Lys Arg Leu Ala
                                     155
                   150
Val Tyr Gln Ala Gly Ala Arg Glu Gly Ala Glu Arg Gly Val Ser Ala
                                  170
               165
Ile Arg Glu Arg Leu Gly Pro Leu Val Glu Gln Gly Arg Val Arg Ala
                              185
Ala Thr Val Gly Ser Leu Ala Ser Gln Pro Leu Gln Glu Arg Ala Gln
                           200
Ala Leu Gly Glu Arg Leu Arg Ala Arg Met Glu Glu Met Gly Ser Arg
                      215
 Thr Arg Asp Arg Leu Asp Glu Val Lys Glu Gln Val Ala Glu Val Arg
                                     235
                  230
Ala Lys Leu Glu Glu Gln Ala Gln Gln Ile Ser Leu Gln Ala Glu Ala
                                 250
               245
 Phe Gln Ala Arg Leu Lys Ser Trp Phe Glu Pro Leu Val Glu Asp Met
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Gln Arg Gln Trp Ala Gly Leu Val Glu Lys Val Gln Ala Ala Val Gly
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 Ala Ser Thr Ala Pro Val Pro Ser Asp Asn His
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<213> rat

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75
                   70
Thr Arg Ala Arg Leu Thr Lys Glu Val Gln Ala Ala Gln Ala Arg Leu
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Gly Ala Asp Met Glu Asp Leu Arg Asn Arg Leu Gly Gln Tyr Arg Asn
                               105
Glu Val Asn Thr Met Leu Gly Gln Ser Thr Glu Glu Leu Arg Ser Arg
                           120
       115
Leu Ser Thr His Leu Arg Lys Met Arg Lys Arg Leu Met Arg Asp Ala
                                            140
                       135
Asp Asp Leu Gln Lys Arg Leu Ala Val Tyr Lys Ala Gly Ala Gln Glu
                                       155
                   150
Gly Ala Glu Arg Gly Val Ser Ala Ile Arg Glu Arg Leu Gly Pro Leu
                                    170
                165
Val Glu Gln Gly Arg Gln Arg Thr Ala Asn Leu Arg Trp Arg Arg Pro
                               185
Ala Pro Arg Asp Arg Ala Gln Ala Leu Ser Asp Arg Ile Arg Gly Arg
                           200
Leu Glu Glu Val Gly Asn Gln Ala Arg Asp Arg Leu Glu Glu Val Arg
                                           220
                        215
Glu Gln Met Glu Glu Val Arg Ser Lys Met Glu Glu Gln Thr Gln Gln
                                        235
                   230
Ile Arg Leu Gln Ala Glu Ile Phe Gln Ala Arg Ile Lys Gly Trp Phe
                                   250
Glu Pro Leu Val Glu Asp Met Gln Arg Gln Trp Ala Asn Leu Met Glu
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Lys Ile Gln Ala Ser Val Ala Thr Asn Ser Ile Ala Ser Thr Thr Val
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Pro Leu Glu Asn Gln
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Pro Trp Glu Gln Ala Leu Asn Arg Phe Trp Asp Tyr Leu Arg Trp Val
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Gln Thr Leu Ser Asp Gln Val Gln Glu Glu Leu Gln Ser Ser Gln Val
Thr Gln Glu Leu Thr Ala Leu Met Glu Asp Thr Met Thr Glu Val Lys
                        55
Ala Tyr Lys Lys Glu Leu Glu Glu Gln Leu Gly Pro Val Ala Glu Glu
                                        75
                    70
Thr Arg Ala Arg Leu Gly Lys Glu Val Gln Ala Ala Gln Ala Arg Leu
                                    90
Gly Ala Asp Met Glu Asp Leu Arg Asn Arg Leu Gly Gln Tyr Arg Asn
                                105
            100
 Glu Val His Thr Met Leu Gly Gln Ser Thr Glu Glu Ile Arg Ala Arg
                                                125
                            120
 Leu Ser Thr His Leu Arg Lys Met Arg Lys Arg Leu Met Arg Asp Ala
                                             140
                         135
 Asp Asp Leu Gln Lys Arg Leu Ala Val Tyr Lys Ala Gly Ala Arg Glu
                    150
                                         155
 Gly Ala Glu Arg Gly Val Ser Ala Ile Arg Glu Arg Leu Gly Pro Leu
                                    170
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Val Glu Gln Gly Arg Gln Arg Thr Ala Asn Leu Gly Ala Gly Ala Ala 185 180 Gln Pro Leu Arg Asp Arg Ala Gln Ala Phe Gly Asp Arg Ile Arg Gly 200 Arg Leu Glu Glu Val Gly Asn Gln Ala Arg Asp Arg Leu Glu Glu Val 215 Arg Glu His Met Glu Glu Val Arg Ser Lys Met Glu Glu Gln Thr Gln 235 230 Gln Ile Arg Leu Gln Ala Glu Ile Phe Gln Ala Arg Leu Lys Gly Trp 250 245 Phe Glu Pro Ile Val Glu Asp Met His Arg Gln Trp Ala Asn Leu Met 265 Glu Lys Ile Gln Ala Ser Val Ala Thr Asn Pro Ile Ile Thr Pro Val 280 Ala Gln Glu Asn Gln 290 <210> 6 <211> 280 <212> PRT <213> GUINEA PIG <400> 6 Asp Val Glu Pro Glu Val Glu Val Arg Glu Pro Ala Val Trp Gln Ser Gly Gln Pro Trp Glu Leu Ala Leu Ser Arg Phe Trp Asp Tyr Leu Arg 25 Trp Val Gln Thr Leu Ser Asp Gln Val Gln Glu Glu Leu Leu Ser Asn Gln Val Thr Gln Glu Leu Thr Leu Leu Ile Glu Asp Thr Met Lys Glu 55 Val Lys Ala Tyr Lys Ala Glu Leu Glu Lys Glu Leu Gly Pro Val Ala Glu Asp Thr Lys Ala Arg Leu Ala Lys Glu Leu Gln Ala Ala Gln Ala 90 85 Arg Leu Gly Ala Asp Met Glu Glu Val Arg Asn Arg Leu Ser Gln Tyr Arg Ser Glu Val Gln Ala Met Leu Gly Gln Ser Ser Glu Glu Leu Arg 120 Ala Arg Leu Thr Ser His Pro Arg Lys Met Lys Arg Arg Leu Gln Arg 135 Asp Ile Asp Glu Leu Gln Lys Arg Met Ala Val Tyr Lys Ala Gly Ala 150 155 Gln Glu Gly Ala Glu Arg Gly Val Ser Ala Ile Arg Glu Arg Leu Gly 170 165 Ser Leu Ile Glu Gln Gly Arg Leu Gln Ala Leu Ala Ser Gln Pro Leu 185 180 Gln Glu Arg Ala Gln Ala Trp Gly Glu Gln Met Arg Gly Arg Leu Glu 200 Lys Val Gly Ser Gln Ala Arg Asp Arg Leu Glu Glu Val Arg Glu Gln 215 220 Met Glu Glu Val Arg Val Lys Val Glu Glu Gln Ala Glu Ala Phe Gln 235 230 Ala Arg Leu Lys Ser Trp Phe Glu Pro Met Met Glu Asp Met Arg Arg 250 245 Gln Trp Ala Glu Leu Ile Gln Lys Val Gln Val Ala Val Gly Ala Ser 265 Thr Ser Ala Pro Ser Gln Glu Pro

275 280

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<213> rabbit
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Gly Gln Pro Trp Glu Leu Ala Leu Gly Arg Phe Trp Asp Tyr Leu Arg
                               25
Trp Val Gln Ser Leu Ser Asp Gln Val Gln Glu Leu Leu Ser Ser
                           40
Gln Val Thr Gln Glu Leu Thr Met Leu Met Glu Glu Thr Met Lys Glu
                       55
Val Lys Ala Tyr Lys Ser Glu Leu Glu Glu Gln Leu Ser Pro Met Ala
                   70
                                       75
Gln Glu His Arg Ala Arg Leu Ser Lys Glu Leu Gln Val Ala Gly Ala
                                   90
               85
Leu Glu Ala Asp Met Glu Asp Val Cys Asn Arg Leu Ala Gln Tyr Arg
                               105
Gly Glu Ala Gln Ala Met Leu Gly Gln Ser Thr Glu Glu Leu Ala Arg
                           120
Ala Phe Ser Ser His Leu Arg Lys Leu Arg Lys Arg Leu Leu Arg Asp
                                           140
                       135
Ala Glu Asp Leu Gln Lys Arg Met Ala Val Tyr Gly Ala Gly Ala Arg
                                       155
                   150
Glu Gly Ala Glu Arg Gly Val Ser Ala Val Arg Glu Arg Leu Gly Ser
               165
                                   170
Arg Leu Glu Arg Gly Arg Leu Arg Val Ala Thr Val Gly Thr Leu Ala
                               185
Gly Arg Pro Leu Arg Glu Arg Ala Gln Ala Trp Gly Glu Arg Leu Arg
                           200
Gly His Leu Glu Glu Val Gly Ser Arg Ala Arg Asp Arg Leu Asn Glu
                                           220
                       215
Val Arg Glu Gln Val Glu Glu Val Arg Val Lys Val Glu Gln Ala
                                        235
                   230
Pro Gln Met Arg Leu Gln Ala Glu Ala Phe Gln Ala Arg Leu Lys Ser
                                    250
Trp Phe Glu Pro Leu Val Glu Asp Met Gln Arg Gln Trp Ala Gly Leu
                               265
Val Glu Lys Leu Gln Ala Ala Met Pro Ser Lys Ala Pro Ala Ala Ala
       275
                           280
Pro Ile Glu Asn Gln
    290
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<211> 298
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<213> cow
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Pro Arg Gly Lys Asp Ser Gln Pro Trp Glu Gln Ala Leu Gly Arg Phe
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Trp Asp Tyr Leu Arg Trp Val Gln Thr Leu Ser Asp Gln Val Gln Glu Glu Leu Leu Asn Thr Gln Val Ile Gln Glu Leu Thr Ala Leu Met Glu Glu Thr Met Lys Glu Val Lys Ala Tyr Lys Glu Glu Leu Glu Gly Gln 70 Leu Gly Pro Met Ala Gln Glu Thr Gln Ala Arg Val Ser Lys Glu Leu Gln Ala Ala Gln Ala Arg Leu Gly Ser Asp Met Glu Asp Leu Arg Asn 105 Arg Leu Ala Gln Tyr Arg Ser Glu Val Gln Ala Met Leu Gly Gln Ser 120 Thr Glu Glu Leu Arg Ala Arg Met Ala Ser His Leu Arg Lys Leu Pro 135 Lys Arg Leu Leu Arg Asp Ala Asp Asp Leu Lys Lys Arg Leu Ala Val 150 155 Tyr Gln Ala Gly Ala Ser Glu Gly Ala Glu Arg Ser Leu Ser Ala Ile 165 170 Arg Glu Arg Phe Gly Pro Leu Val Glu Gln Gly Gln Ser Arg Ala Ala 185 Thr Leu Ser Thr Leu Ala Gly Gln Pro Leu Leu Glu Arg Ala Glu Ala 200 205 Trp Arg Gln Lys Leu His Gly Arg Leu Glu Glu Val Gly Val Arg Ala 215 Gln Asp Arg Leu Asp Lys Ile Arg Gln Gln Leu Glu Glu Val His Ala 230 235 Lys Val Glu Glu Gln Gly Asn Gln Met Arg Leu Gln Ala Glu Ala Phe 245 250 Gln Ala Arg Leu Arg Ser Trp Phe Glu Pro Leu Val Glu Asp Met Gln 265 Arg Gln Trp Ala Gly Leu Val Glu Lys Val Gln Leu Ala Leu Arg Pro 280 Ser Pro Thr Ser Pro Pro Ser Glu Asn His 290 295

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<213> dog

<400> 9

Lys Val Gln Gln Glu Leu Glu Pro Glu Ala Gly Trp Gln Thr Gly Gln 10 Pro Trp Glu Ala Ala Leu Ala Arg Phe Trp Asp Tyr Leu Arg Trp Val 25 Gln Thr Leu Ser Asp Gln Val Gln Glu Gly Val Leu Asn Thr Gln Val 40 Thr Gln Glu Leu Thr Ala Leu Met Asp Glu Thr Met Lys Glu Val Lys 55 60 Ala Tyr Lys Ala Glu Leu Asp Glu Gln Leu Gly Pro Met Thr Ser Glu 75 Thr Gln Ala Arg Val Ala Lys Glu Leu Gln Ala Ala Gln Ala Arg Leu 90 Arg Ala Asp Met Glu Asp Val Arg Asn Arg Leu Thr Gln Tyr Arg Gly 105 Glu Leu Gln Ala Met Leu Gly Gln Ser Ser Glu Glu Leu Arg Ala Arg 120 Phe Ala Ser His Met Arg Lys Leu Arg Lys Arg Val Leu Arg Asp Ala

140 135 130 Glu Asp Leu Gln Arg Arg Leu Ala Val Tyr Lys Ala Gly Val Arg Glu 155 150 Gly Ala Glu Arg Ser Val Ser Ser Ile Arg Glu Arg Leu Trp Pro Leu 165 170 Leu Glu Gln Ala Arg Glu Arg Asn Ala Lys Val Gly Ala Leu Ala Thr 185 Gln Pro Leu Glu Arg Ala Asp Ala Trp Gly Gln Gln Leu Arg Gly . 200 Gln Leu Glu Glu Met Ser Ser Arg Ala Arg Gly His Leu Glu Glu Met 215 220 Arg Glu Gln Ile Gln Glu Val Arg Val Lys Met Glu Glu Gln Ala Asp 230 235 Gln Ile Arg Gln Lys Ala Glu Ala Phe Gln Ala Arg Leu Lys Ser Trp 245 250 Phe Glu Pro Leu Leu Glu Asp Met Gln Arg Gln Trp Asp Gly Leu Val 265 Glu Lys Val Gln Ala Ala Val Ala Thr Ile Pro Thr Ser Lys Pro Val 280 Glu Glu Pro 290 <210> 10 <211> 291 <212> PRT <213> sea lion <400> 10 Glu Leu Glu Gln Glu Val Glu Pro Glu Ala Gly Trp Gln Ala Gly Gln 5 10 Pro Trp Glu Leu Ala Leu Ala Arg Phe Trp Asp Tyr Leu Arg Trp Val 25 Gln Thr Leu Ser Asp Gln Val Gln Glu Glu Val Leu Ser Asn Gln Val 40 Thr Gln Glu Leu Thr Thr Leu Met Glu Glu Thr Met Lys Glu Ile Lys 55 60 Ala Tyr Arg Ala Glu Leu Glu Glu Gln Leu Gly Pro Met Ala Ser Glu 70 75 Thr Gln Ala Arg Val Ala Lys Glu Leu Gln Ala Ala Gln Ala Arg Leu 85 90 Arg Ser Asp Met Glu Asp Val Arg Thr Arg Leu Ser Gln Tyr Arg Gly 105 Glu Val Gln Ala Met Leu Gly Gln Ser Thr Glu Glu Leu Arg Ala Arg 120 Phe Ala Ser His Met Arg Lys Leu Arg Lys Arg Val Leu Arg Asp Ala 135 140 Glu Asp Leu Gln Lys Arg Leu Ala Val Tyr Arg Ala Gly Val Arg Glu 155 150 Gly Ala Glu Arg Ser Val Ser Thr Ile Arg Glu Arg Leu Trp Pro Leu 165 170 Leu Glu Gln Ala Arg Thr Arg His Ala Lys Val Asp Ala Leu Ala Thr 185 Gln Pro Leu Arg Glu Arg Val Asn Ala Leu Gly Gln Gln Leu Arg Gly 200 Arg Leu Glu Glu Val Gly Ser Arg Ala Arg Ser His Leu Asp Glu Val 215 220 Arq Glu Gln Met Glu Glu Val Gln Ala Lys Met Glu Glu Gln Ala Asn

235

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Gln Met Arg Gln Gln Ala Glu Ala Phe Gln Ala Arg Leu Lys Gly Trp
               245
Phe Glu Pro Leu Val Glu Asp Met Gln Arg Gln Trp Ala Val Leu Val
                          265
Glu Lys Val Gln Ala Ala Val Gly Thr Ser Pro Thr Thr Pro Pro Val
       275
                           280
Glu Thr Lys
   290
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Glu Pro Lys Arg
1
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